

AMENDMENT

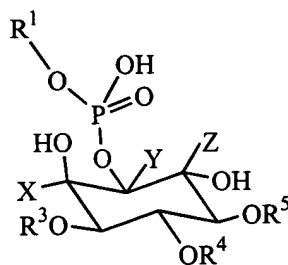
Amendments to the Claims

The present document amends claims 21, 22, 24, 25, 26, and 53, and adds claims 55-56.

According to 37 C.F.R. § 1.121(c), after entry of the present amendment, the status of the claims in the case is as follows:

Claims 1-20 canceled.

21. (Currently amended) A substantially purified sphingo-phosphoinositol analogue of a phosphoinositide compound that comprises at least a first stable or radioactive isotope label within the inositol, ceramide or sphingosine residue of said phosphoinositide compound; wherein said stable or radioactive isotope label is selected from the group consisting of ^2H , ^3H , ^{32}P , ^{33}P and ^{35}S and wherein said phosphoinositide compound has the *myo*-inositol-based structure:



wherein:

R^1 = Ceramide residue or derivative thereof of ceramide residue, or

Sphingosine residue or derivative thereof of sphingosine residue;

R^3 , R^4 , R^5 = H or $\text{Q}(\text{T})(\text{OH})_2$;

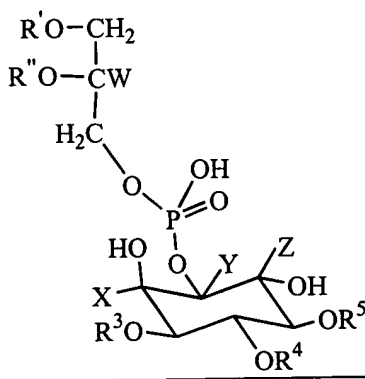
Q = P, ^{32}P or ^{33}P ;

T = O, S or ^{35}S ;

W, X, Y, Z = ^2H , ^3H or H; and

wherein said structure contains at least one ^2H , ^3H , ^{32}P , ^{33}P or ^{35}S as isotopic label.

22. (Currently amended) A substantially purified C-phosphonate analogue of a phosphoinositide compound that comprises at least a first stable or radioactive isotope label within the inositol or glycerol residue of said phosphonate analogue of the phosphoinositide compound; wherein said stable or radioactive isotope label is selected from the group consisting of ^2H , ^3H , ^{32}P , ^{33}P and ^{35}S and wherein said phosphoinositide compound has the *myo*-inositol-based structure:



wherein:

R', R'' = fattyacyl, alkyl or H;

R³, R⁴, R⁵ = H or Q(T)(OH)₂;

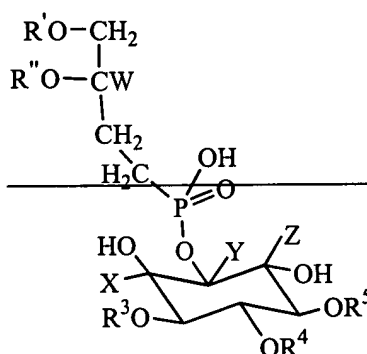
Q = P, ^{32}P or ^{33}P ;

T = O, S or ^{35}S ;

W, X, Y, Z = ^2H , ^3H or H; and

wherein said structure contains at least one ^2H , ^3H , ^{32}P , ^{33}P or ^{35}S as isotopic label, and
wherein an O-P bond of phosphate moiety of said phosphoinositide compound structure is
replaced by a C-P bond.

~~— A substantially purified C-phosphonate analogue of a phosphoinositide compound that~~
~~comprises at least a first stable or radioactive isotope label within the inositol or the~~
~~C-phosphonate phosphatidyl residue of said phosphoinositide compound; wherein said stable or~~
~~radioactive isotope label is selected from the group consisting of ^2H , ^3H , ^{32}P , ^{33}P and ^{35}S and~~
~~wherein said phosphoinositide compound has the *myo*-inositol based structure:~~



~~— wherein:~~

~~— R' , R'' = fattyacyl, alkyl or H;~~

~~— R^3 , R^4 , R^5 = H or $\text{Q}(\text{T})(\text{OH})_2$;~~

~~— $\text{Q} = \text{P}$, ^{32}P or ^{33}P ;~~

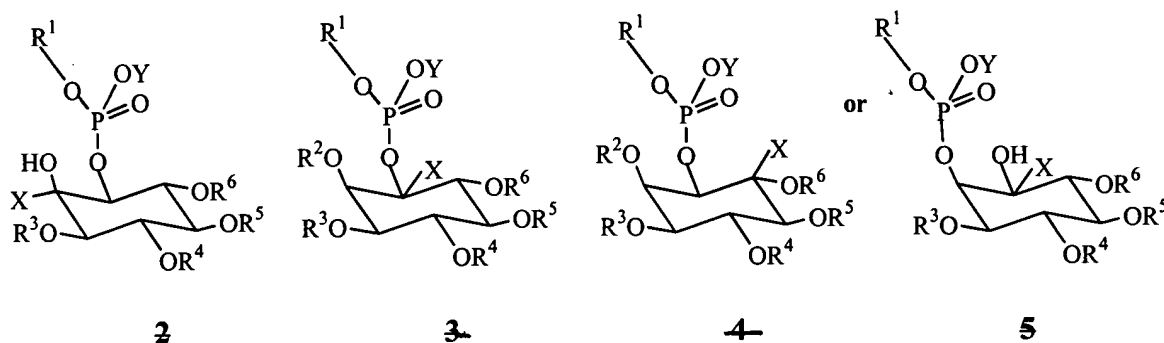
~~— $\text{T} = \text{O}$, S or ^{35}S ;~~

~~— W , X , Y , $\text{Z} = ^2\text{H}$, ^3H or H; and~~

~~— wherein said structure contains at least one ^2H , ^3H , ^{32}P , ^{33}P or ^{35}S as isotopic label.~~

23. (Original) The C-phosphonate phosphoinositide compound of claim 22, wherein said phosphoinositide compound comprises at least a first (poly)unsaturated fattyacyl residue.

24. (Currently amended) A synthetic intermediate of an isotopically labelled sphingo-phosphoinositol analogue of a phosphoinositide compound, said synthetic intermediate comprising temporary protecting groups at hydroxyl, nitrogen and phosphate positions other than the position into which the isotopic label is to be introduced; wherein said synthetic intermediate has one of the *myo*-inositol-based structures:



wherein:

$X = H, {}^2H$ or 3H ; $Y = \text{alkyl}, CH_3, H$ or (O protecting group);

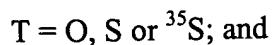
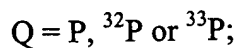
$R^1 = \text{Ceramide residue or derivative thereof of ceramide residue, or}$

$\text{Sphingosine residue or derivative thereof of sphingosine residue;}$

$R^3, R^4, R^5 = (\text{OH protecting group}), (Q(T)(\text{O protecting group})_2),$

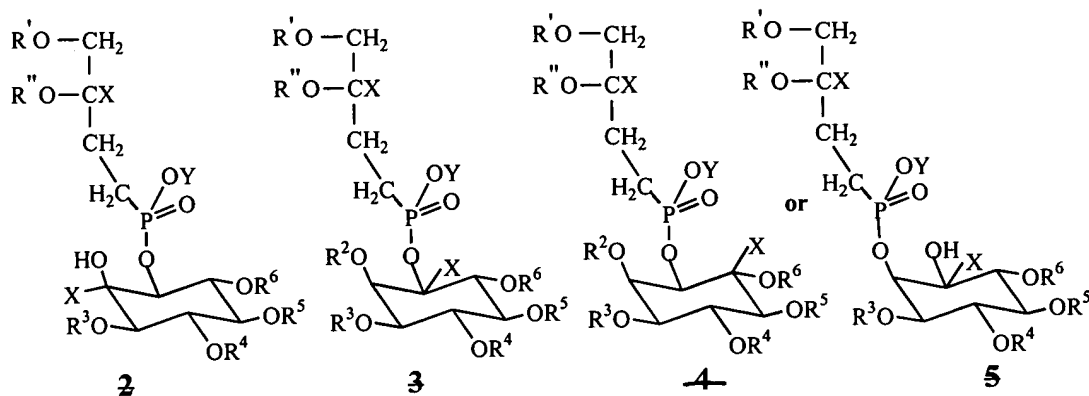
$(Q(T)(\text{OH})(\text{O protecting group}))$ or $(Q(T)(\text{OH})_2)$;

$R^2, R^6 = H$ or (OH protecting group);



wherein said structure contains at least one ${}^2\text{H}$, ${}^3\text{H}$, ${}^{32}\text{P}$, ${}^{33}\text{P}$ or ${}^{35}\text{S}$ as isotopic label.

25. (Currently amended) A synthetic intermediate of an isotopically labelled C-phosphonate analogue of a phosphoinositide compound, said synthetic intermediate comprising temporary protecting groups at hydroxyl, phosphonate and phosphate positions other than the position into which the isotopic label is to be introduced; wherein said synthetic intermediate has one of the *myo*-inositol-based structures:



wherein:

$X = \text{H}, {}^2\text{H} \text{ or } {}^3\text{H}; Y = \text{alkyl}, \text{CH}_3, \text{H} \text{ or } (\text{O protecting group});$

$R', R'' = \text{fattyacyl}, \text{alkyl} \text{ or } \text{H};$

$R^3, R^4, R^5 = (\text{OH protecting group}), (\text{Q(T)}(\text{O protecting group})_2),$

$(\text{Q(T)}(\text{OH})(\text{O protecting group}) \text{ or } (\text{Q(T)}(\text{OH})_2);$

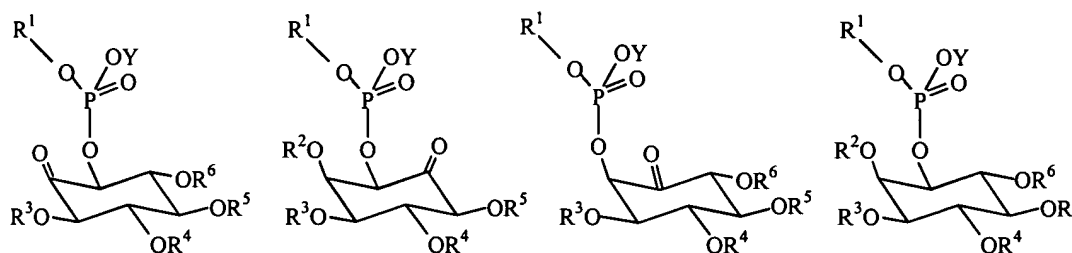
$R^2, R^6 = \text{H} \text{ or } (\text{OH protecting group});$

$Q = P, {}^{32}\text{P} \text{ or } {}^{33}\text{P};$

T = O, S or ^{35}S ; and

wherein said structure contains at least one ^2H , ^3H , ^{32}P , ^{33}P or ^{35}S as isotopic label.

26. (Currently amended) A synthetic precursor of a synthetic intermediate of an isotopically labelled sphingo-phosphoinositol analogue of a phosphoinositide compound, wherein said synthetic precursor has a ketone group at the position into which an isotopic ^2H or ^3H label is to be introduced; wherein said synthetic precursor has one of the structures:



wherein:

Y = alkyl, CH₃ or H;

R¹ = Ceramide residue or derivative thereof of ceramide residue, or

Sphingosine residue or derivative thereof of sphingosine residue;

R³, R⁴, R⁵ = (OH protecting group), (Q(T)(O protecting group)₂),

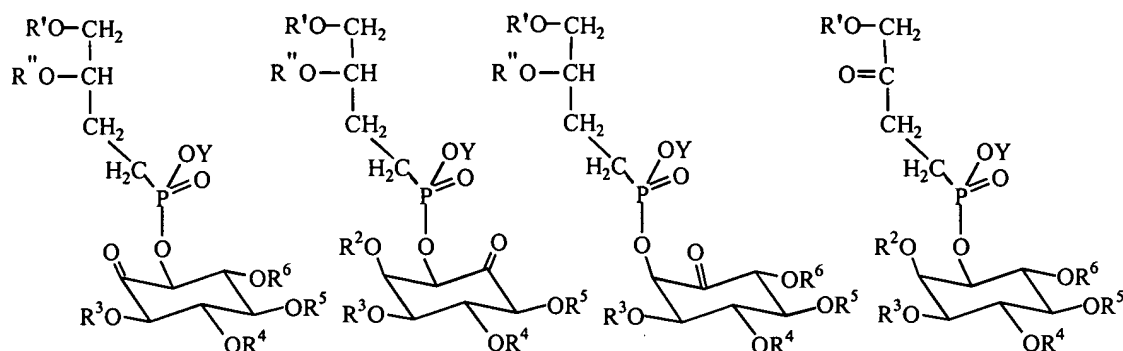
(Q(T)(OH)(O protecting group) or (Q(T)(OH)₂);

R², R⁶ = H or (OH protecting group); and

Q = P, ^{32}P or ^{33}P ; and

T = O, S or ^{35}S .

27. (Original) A synthetic precursor of a synthetic intermediate of an isotopically labelled C-phosphonate analogue of a phosphoinositide compound, wherein said synthetic precursor has a ketone group at the position into which an isotopic ^2H or ^3H label is to be introduced; wherein said synthetic precursor has one of the structures:



wherein:

Y = alkyl, CH_3 or H;

R' , R'' = fattyacyl, alkyl or H;

R^3 , R^4 , R^5 = (OH protecting group), $(\text{Q}(\text{T})(\text{O protecting group})_2)$,

$(\text{Q}(\text{T})(\text{OH})(\text{O protecting group}))$ or $(\text{Q}(\text{T})(\text{OH})_2)$;

R^2 , R^6 = H or (OH protecting group); and

Q = P, ^{32}P or ^{33}P ; and

T = O, S or ^{35}S .

28. (Original) The synthetic intermediate of claim 25, wherein said synthetic intermediate comprises at least a first (poly)unsaturated fattyacyl residue.

29. (Original) The synthetic precursor of claim 27, wherein said synthetic precursor comprises at least a first (poly)unsaturated fattyacyl residue.

30. (Original) The sphingo-phosphoinositol phosphoinositide compound of claim 21, wherein said phosphoinositide compound further comprises at least a second stable or radioactive isotope label within the ceramide or sphingosine residues of said sphingo-phosphoinositol phosphoinositide compound.

31. (Original) The C-phosphonate phosphoinositide compound of claim 22, wherein said phosphoinositide compound further comprises at least a second stable or radioactive isotope label within the alkyl or fattyacyl residues of said C-phosphonate phosphoinositide compound.

32. (Original) The sphingo-phosphoinositol phosphoinositide compound of claim 21, wherein said phosphoinositide compound has a structure based on 1D-*myo*-inositol.

33. (Original) The sphingo-phosphoinositol phosphoinositide compound of claim 21, wherein said phosphoinositide compound has a structure based on 1L-*myo*-inositol.

34. (Original) The C-phosphonate phosphoinositide compound of claim 22, wherein said phosphoinositide compound has a structure based on 1D-*myo*-inositol.

35. (Original) The C-phosphonate phosphoinositide compound of claim 22, wherein said phosphoinositide compound has a structure based on 1L-*myo*-inositol.

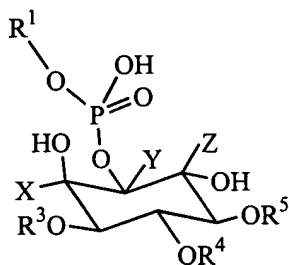
36. (Original) The synthetic intermediate of claim 24, wherein said synthetic intermediate has a structure based on 1D-*myo*-inositol.
37. (Original) The synthetic intermediate of claim 24, wherein said synthetic intermediate has a structure based on 1L-*myo*-inositol.
38. (Original) The synthetic intermediate of claim 25, wherein said synthetic intermediate has a structure based on 1D-*myo*-inositol.
39. (Original) The synthetic intermediate of claim 25, wherein said synthetic intermediate has a structure based on 1L-*myo*-inositol.
40. (Original) The synthetic precursor of claim 26, wherein said synthetic precursor has a structure based on 1D-*myo*-inositol.
41. (Original) The synthetic precursor of claim 26, wherein said synthetic precursor has a structure based on 1L-*myo*-inositol.
42. (Original) The synthetic precursor of claim 27, wherein said synthetic precursor has a structure based on 1D-*myo*-inositol.

43. (Original) The synthetic precursor of claim 27, wherein said synthetic precursor has a structure based on 1L-*myo*-inositol.
44. (Original) The C-phosphonate phosphoinositide compound of claim 22, wherein said phosphoinositide compound has a structure based on *sn*-glycero-3-phospho as glycerol residue.
45. (Original) The C-phosphonate phosphoinositide compound of claim 22, wherein said phosphoinositide compound has a structure based on *sn*-glycero-1-phospho as glycerol residue.
46. (Original) The C-phosphonate phosphoinositide compound of claim 22, wherein said phosphoinositide compound has a structure based on *rac*-glycero-3-phospho as glycerol residue.
47. (Original) The synthetic intermediate of claim 25, wherein said synthetic intermediate has a structure based on *sn*-glycero-3-phospho as glycerol residue.
48. (Original) The synthetic intermediate of claim 25, wherein said synthetic intermediate has a structure based on *sn*-glycero-1-phospho as glycerol residue.
49. (Original) The synthetic intermediate of claim 25, wherein said synthetic intermediate has a structure based on *rac*-glycero-3-phospho as glycerol residue.
50. (Original) The synthetic precursor of claim 27, wherein said synthetic precursor has a structure based on *sn*-glycero-3-phospho as glycerol residue.

51. (Original) The synthetic precursor of claim 27, wherein said synthetic precursor has a structure based on *sn*-glycero-1-phospho as glycerol residue.

52. (Original) The synthetic precursor of claim 27, wherein said synthetic precursor has a structure based on *rac*-glycero-3-phospho as glycerol residue.

53. (Currently amended) A substantially purified sphingo-phosphoinositol phosphoinositide compound that comprises at least a first stable or radioactive isotope label within the inositol, ceramide or sphingosine residue of said phosphoinositide compound; wherein said stable or radioactive isotope label is selected from the group consisting of ^2H , ^3H , ^{32}P , ^{33}P and ^{35}S ; wherein said phosphoinositide compound has the *myo*-inositol-based structure:



wherein:

R^1 = Ceramide residue or derivative thereof of ceramide residue, or

Sphingosine residue or derivative thereof of sphingosine residue;

$\text{R}^3, \text{R}^4, \text{R}^5 = \text{H}$ or $\text{Q}(\text{T})(\text{OH})_2$;

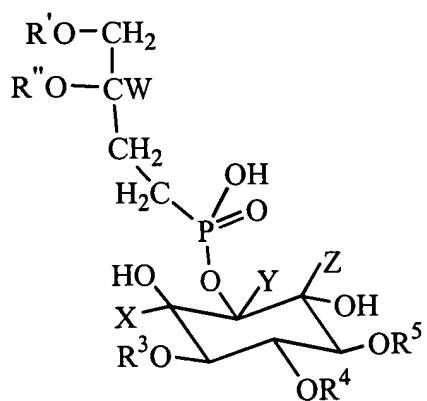
$\text{Q} = \text{P}, ^{32}\text{P}$ or ^{33}P ;

$\text{T} = \text{O}, \text{S}$ or ^{35}S ;

$\text{W}, \text{X}, \text{Y}, \text{Z} = ^2\text{H}, ^3\text{H}$ or H ; and

wherein said structure contains at least one ^2H , ^3H , ^{32}P , ^{33}P or ^{35}S as isotopic label and further comprises temporary protecting groups at hydroxyl and phosphate positions other than the position of at least a first stable or radioactive ^2H and ^3H isotope label.

54. (Original) A substantially purified C-phosphonate phosphoinositide compound that comprises at least a first stable or radioactive isotope label within the inositol or glycerol residue of said phosphoinositide compound; wherein said stable or radioactive isotope label is selected from the group consisting of ^2H , ^3H , ^{32}P , ^{33}P and ^{35}S ; wherein said phosphoinositide compound has the *myo*-inositol-based structure:



wherein:

$\text{R}', \text{R}'' = \text{fattyacyl, alkyl or H};$

$\text{R}^3, \text{R}^4, \text{R}^5 = \text{H or Q(T)(OH)}_2;$

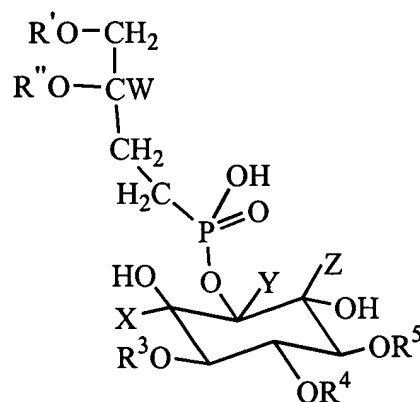
$\text{Q} = \text{P}, ^{32}\text{P or } ^{33}\text{P};$

$\text{T} = \text{O, S or } ^{35}\text{S};$

$\text{W, X, Y, Z} = ^2\text{H}, ^3\text{H or H}; \text{ and}$

wherein said structure contains at least one ^2H , ^3H , ^{32}P , ^{33}P or ^{35}S as isotopic label and further comprises temporary protecting groups at hydroxyl and phosphate positions other than the position of at least a first stable or radioactive ^2H and ^3H isotope label.

55. (New) A C-phosphonate analogue phosphoinositide compound of claim 22 wherein the O-P bond link to glycerol in phosphoinositide structure is replaced by a C-P bond, and wherein the said C-phosphonate analogue phosphoinositide compound has the structure:



wherein:

$\text{R}', \text{R}'' = \text{fattyacyl, alkyl or H};$

$\text{R}^3, \text{R}^4, \text{R}^5 = \text{H or Q(T)(OH)}_2;$

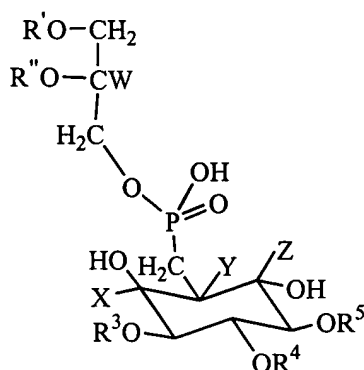
$\text{Q} = \text{P, } ^{32}\text{P or } ^{33}\text{P};$

$\text{T} = \text{O, S or } ^{35}\text{S};$

$\text{W, X, Y, Z} = ^2\text{H, } ^3\text{H or H; and}$

wherein said structure contains at least one ^2H , ^3H , ^{32}P , ^{33}P or ^{35}S as isotopic label.

56. (New) A phosphonate analogue phosphoinositide compound of claim 55 wherein the O-P bond link to inositol in phosphoinositide structure is replaced by a C-P bond, and wherein the said phosphonate analogue phosphoinositide compound has the structure:



wherein:

R' , R'' = fattyacyl, alkyl or H;

R^3 , R^4 , R^5 = H or $Q(T)(OH)_2$;

Q = P, ^{32}P or ^{33}P ;

T = O, S or ^{35}S ;

W , X , Y , Z = 2H , 3H or H; and

wherein said structure contains at least one 2H , 3H , ^{32}P , ^{33}P or ^{35}S as isotopic label.